Appl. No. 10/678,765 Amdt. dated April 14, 2009

Response to Final Office Action of November 14, 2008

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-30. (Canceled)

 (Currently Amended) A method of screening an agent for toxic activity and a pharmacological therapeutie activity in vivo comprising:

administering the agent to a plurality of teleosts in vivo;

detecting in vitro or in situ a change in expression of a protein or mRNA in a specific organ or tissue of the teleost responsive to the agent relative to the expression of the protein or mRNA in the specific organ or tissue of a teleost to which the agent has not been administered, the change in expression indicating toxic activity in at least one tissue or organ of the teleost administered the agent; and

detecting *in vitro* or *in situ* a change in a different teleost administered the agent relative to a control teleost not administered the agent, wherein the change is indicative of the pharmacologicaltherapeutie activity.

- 32. (Canceled)
- 33. (Previously Presented) The method of claim 31, wherein the change in the teleost indicating toxic activity is detected in at least two tissues, at least two organs, or at least one tissue and one organ simultaneously.
 - (Canceled)
- 35. (Previously Presented) The method of claim 31, wherein a response is detected indicating toxic activity in at least two teleosts simultaneously.

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- 36. (Previously Presented) The method of claim 35, wherein each of said at least two teleosts is contained in a separate well of a multi-well plate.
- (Previously Presented) The method of claim 36, wherein the wells of the multi-well plate have a volume of 300 microliters or smaller per well.
- (Previously Presented) The method of claim 36, wherein the wells contain the teleosts in a volume of 50-200 microliters per well.
- 39 (Previously Presented) The method of claim 31, wherein the plurality of teleosts are contained within separate wells of a multi-well plate having a volume of 300 microliters or smaller.
- 40. (Previously Presented) The method of claim 31, wherein the plurality of teleosts are contained within separate wells of a multi-well plate in a volume of 50-200 microliters.
 - 41. (Canceled)
- 42. (Currently Amended) A method of screening an agent for toxic activity *in vivo* comprising:

contacting a living teleost with a test agent, wherein the test agent is added to culture media already containing the teleost, whereby the agent permeates the teleost; and

detecting in vitro or in situ a change in expression of a protein or mRNA in a specific organ or tissue of the teleost responsive to the agent relative to the expression of the protein or mRNA in the specific organ or tissue of a control teleost that has not been contacted with the agent, the change in expression indicating toxic activity in the at least one tissue or organ of the teleost contacted with the agent.

 (Previously Presented) The method of claim 42, wherein the change in expression of the protein or mRNA in the teleost indicating toxic activity is detected over time. Appl. No. 10/678,765 Amdt. dated April 14, 2009

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- 44. (Previously Presented) The method of claim 42, wherein the change in expression of the protein or mRNA in the teleost indicating toxic activity is detected in at least two tissues, at least two organs, or at least one tissue and one organ simultaneously.
- 45. (Previously Presented) The method of claim 44, wherein the change in expression of the protein or mRNA in the teleost indicating toxic activity is over time at predetermined intervals.
- 46. (Previously Presented) The method of claim 42, further comprising contacting at least two teleosts with the agent and detecting a change in expression of the protein or mRNA indicating toxic activity in each of said at least two teleosts simultaneously.
- (Previously Presented) The method of claim 46, wherein each of said at least two teleosts is contained in a well of a multi-well plate.
- 48. (Previously Presented) The method of claim 47, wherein the wells of the multi-well plate have a volume of 300 microliters or smaller per well.
- (Previously Presented) The method of claim 47, wherein the wells contain
 the teleosts in a volume of 50-200 microliters per well.
- 50. (Previously Presented) The method of claim 42, wherein the teleost and the control teleost are contained in separate wells of a single multi-well plate.
- (Previously Presented) The method of claim 50, wherein the wells of the multi-well plate have a volume of 300 microliters or smaller per well.
- 52. (Previously Presented) The method of claim 50, wherein the wells of the multi-well plate have a volume of greater than 300 microliters per well.
- (Previously Presented) The method of claim 42, wherein the teleost is a zebrafish.

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- (Previously Presented) The method of claim 31, wherein the plurality of teleosts are zebrafish.
- 55. (Previously Presented) The method of claim 42, wherein the teleost has a chorion when contacted with the test agent.
- (Previously Presented) The method of claim 31, wherein the plurality of teleosts are wild-type teleosts.
- $\,$ 57. (Previously Presented) The method of claim 42, wherein the teleost is a wild-type teleost.